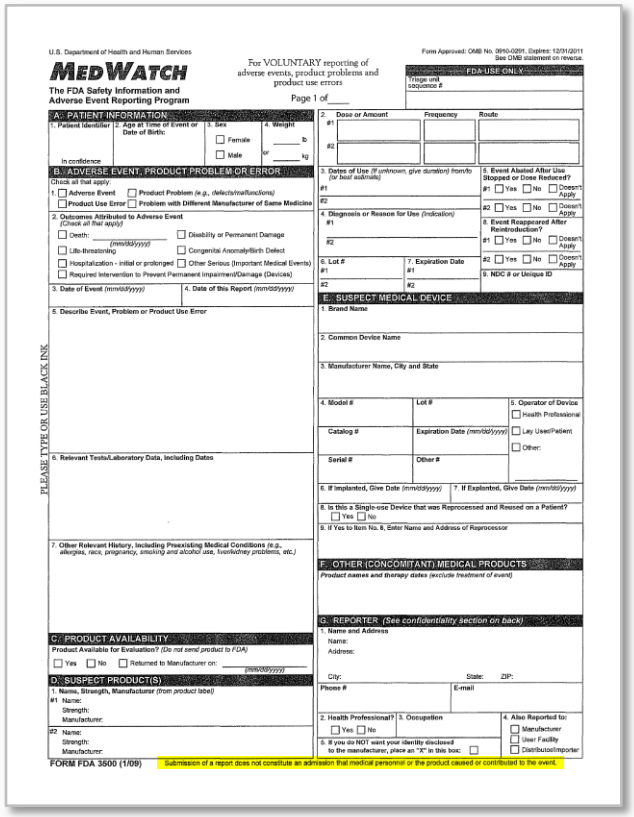
Dr. Weiss's Opinions

- Adverse event reports cannot reliably be used to establish a causal relationship between gabapentin and suicide
- The FDA's AERS database does not support the finding of a signal for completed suicide or suicide attempt
- Dr. Blume's methodology for reviewing AERS data is flawed and not generally accepted
- The information in the AERS database for gabapentin and suicide is unreliable and therefore uninterpretable

Sample MedWatch Form



U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Form Approved: OMB No. 0910-0291, Expires: 12/31/2011
See OMB statement on reverse.

Page 1 of ____

FDA USE ONLY

Triage unit
sequence #

A. PATIENT INFORMATION

1. Patient Identifier / 2. Age at Time of Event or Date of Birth: / 3. Sex: ☐ Female ☐ Male / 4. Weight: _____ lb or _____ kg

In confidence

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☐ Adverse Event ☐ Product Problem (e.g., defects/malfunctions)
☐ Product Use Error ☐ Problem with Different Manufacturer of Same Medicine

2. Outcomes Attributed to Adverse Event (Check all that apply)
☐ Death: _____ (mm/dd/yyyy) ☐ Disability or Permanent Damage
☐ Life-threatening ☐ Congenital Anomaly/Birth Defect
☐ Hospitalization - initial or prolonged ☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. Date of Event (mm/dd/yyyy) / 4. Date of this Report (mm/dd/yyyy)

5. Describe Event, Problem or Product Use Error

6. Relevant Tests/Laboratory Data, including Dates

7. Other Relevant History, including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)

C. PRODUCT AVAILABILITY

Product Available for Evaluation? (Do not send product to FDA)
☐ Yes ☐ No ☐ Returned to Manufacturer on: _____ (mm/dd/yyyy)

D. SUSPECT PRODUCT(S)

1. Name, Strength, Manufacturer (from product label)
#1 Name:
Strength:
Manufacturer:
#2 Name:
Strength:
Manufacturer:

2. Dose or Amount / Frequency / Route
#1
#2

3. Dates of Use (If unknown, give duration) from/to (or best estimate)
#1
#2

4. Diagnosis or Reason for Use (Indication)
#1
#2

5. Event Abated After Use Stopped or Dose Reduced?
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot #
#1
#2

7. Expiration Date
#1
#2

8. Event Reappeared After Reintroduction?
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC # or Unique ID

E. SUSPECT MEDICAL DEVICE

1. Brand Name
2. Common Device Name
3. Manufacturer Name, City and State
4. Model # / Lot # / 5. Operator of Device: ☐ Health Professional ☐ Lay User/Patient ☐ Other:
Catalog # / Expiration Date (mm/dd/yyyy)
Serial # / Other #
6. If Implanted, Give Date (mm/dd/yyyy) / 7. If Explanted, Give Date (mm/dd/yyyy)
8. Is this a Single-use Device that was Reprocessed and Reused on a Patient? ☐ Yes ☐ No
9. If Yes to Item No. 8, Enter Name and Address of Reprocessor

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates (exclude treatment of event)

G. REPORTER (See confidentiality section on back)

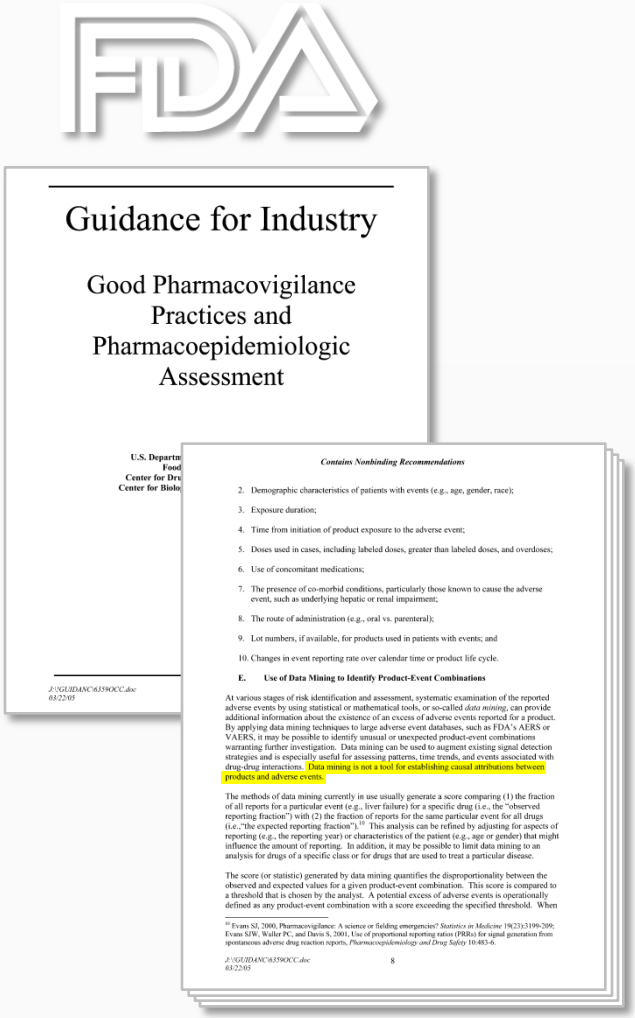
1. Name and Address
Name:
Address:
City: State: ZIP:
Phone # / E-mail
2. Health Professional? ☐ Yes ☐ No / 3. Occupation / 4. Also Reported to: ☐ Manufacturer ☐ User Facility ☐ Distributor/Importer
5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box: ☐

PLEASE TYPE OR USE BLACK INK

FORM FDA 3500 (1/09) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Data Mining Cannot Establish Causation



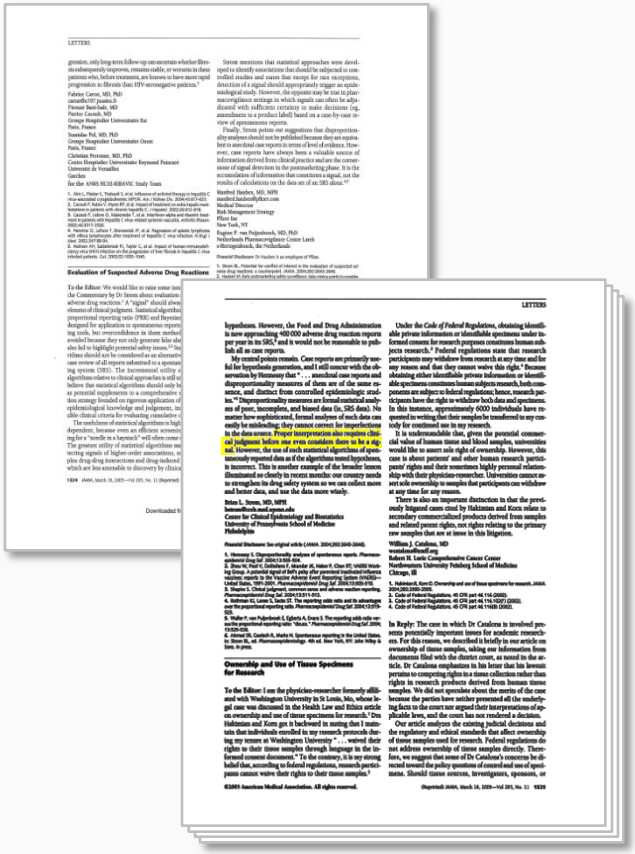
March 2005

Data mining is not a tool for establishing causal attributions between products and adverse events.

Source: March 2005 FDA Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, Pg. 8

Case 3:05-cv-00444 Document 181-2 Filed 04/27/10 Page 3 of 15 PageID #: 4373

Clinical Judgment Necessary For Review of Data Mining

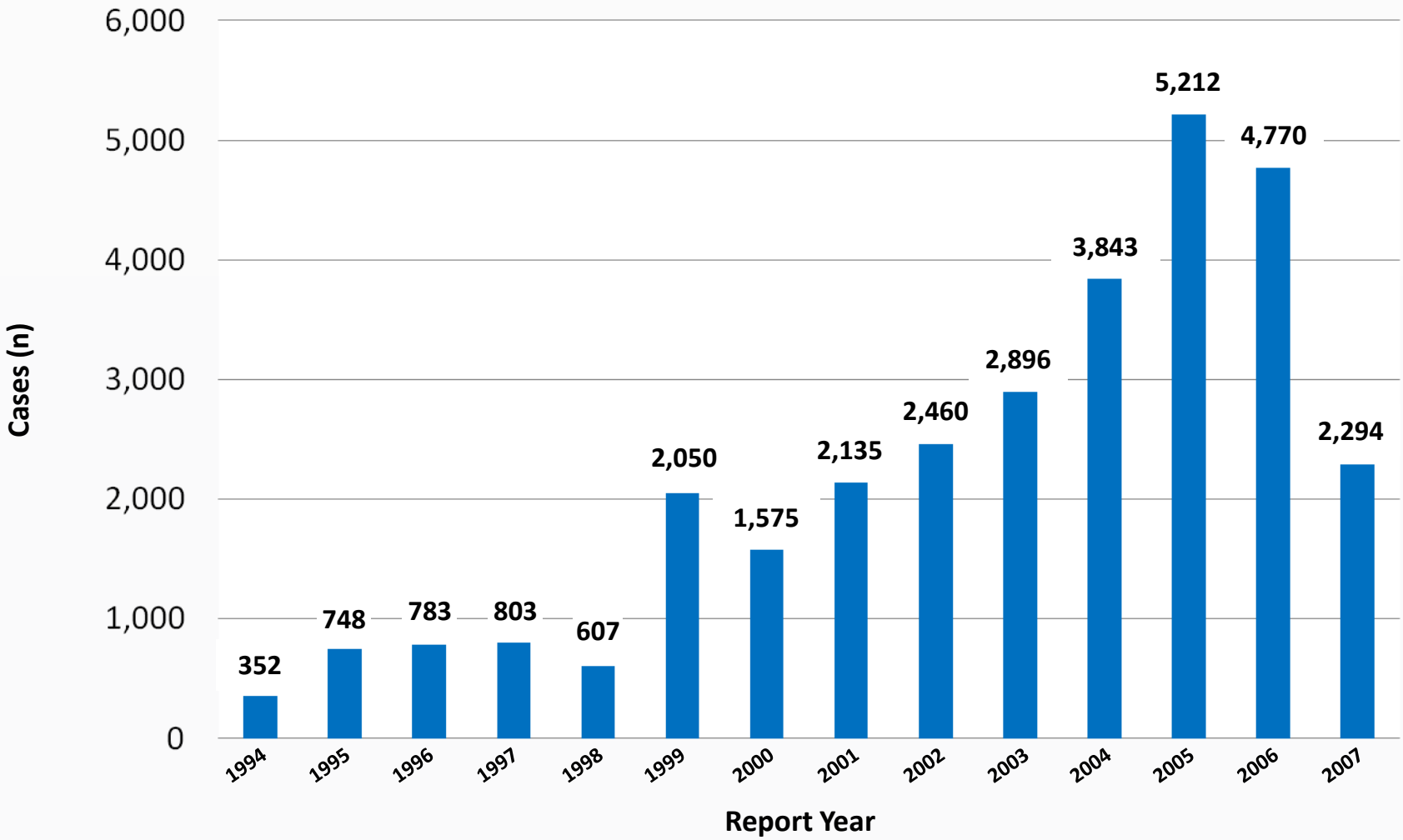


March 2005

Proper interpretation also requires clinical judgment before one even considers there to be a signal.

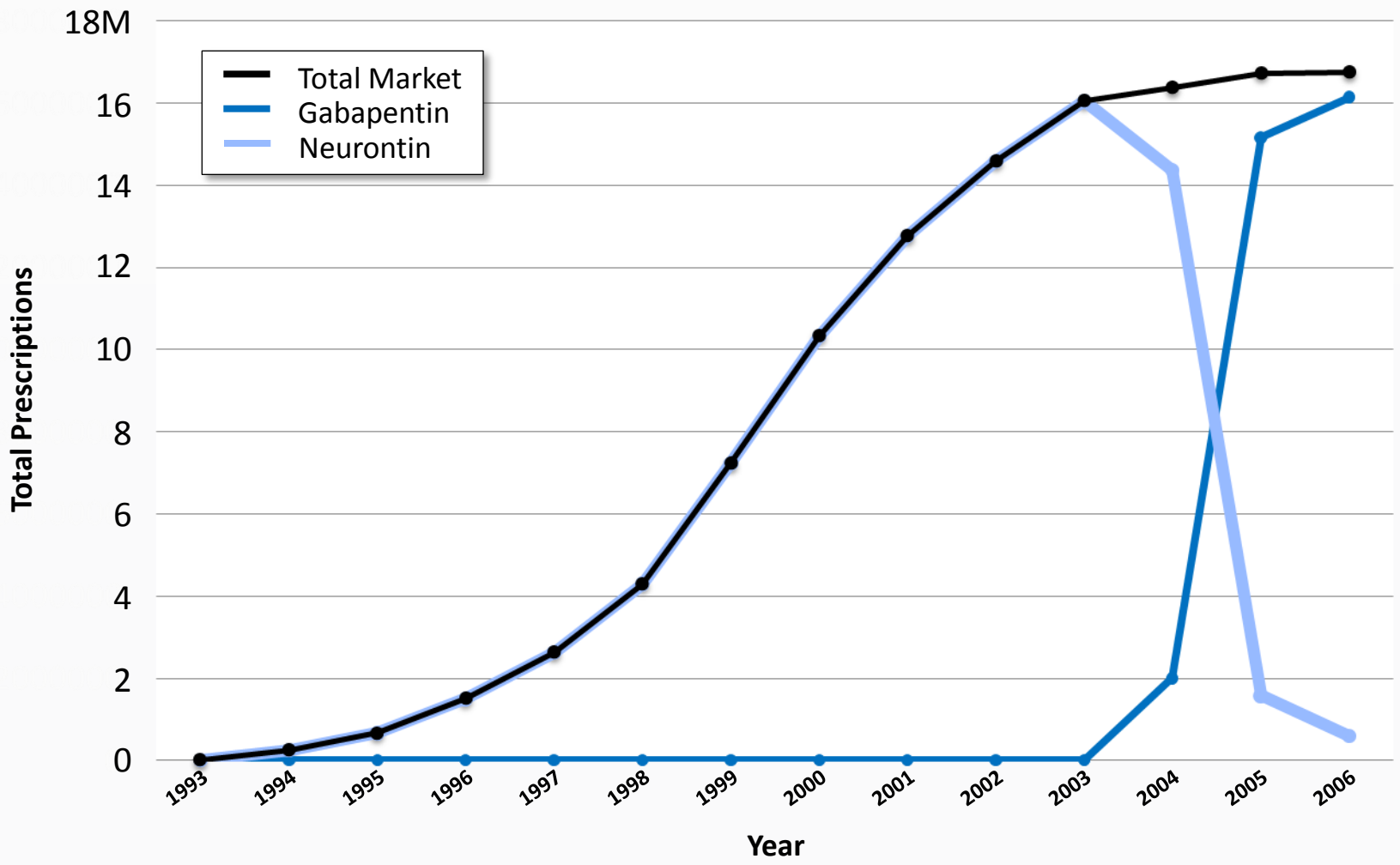
Source: Brian L. Strom, M.D., MPH, Reply to Letter to the Editor, 293 *JAMA* (2005), Pg. 1325

Gabapentin Spontaneous Reports Over Time



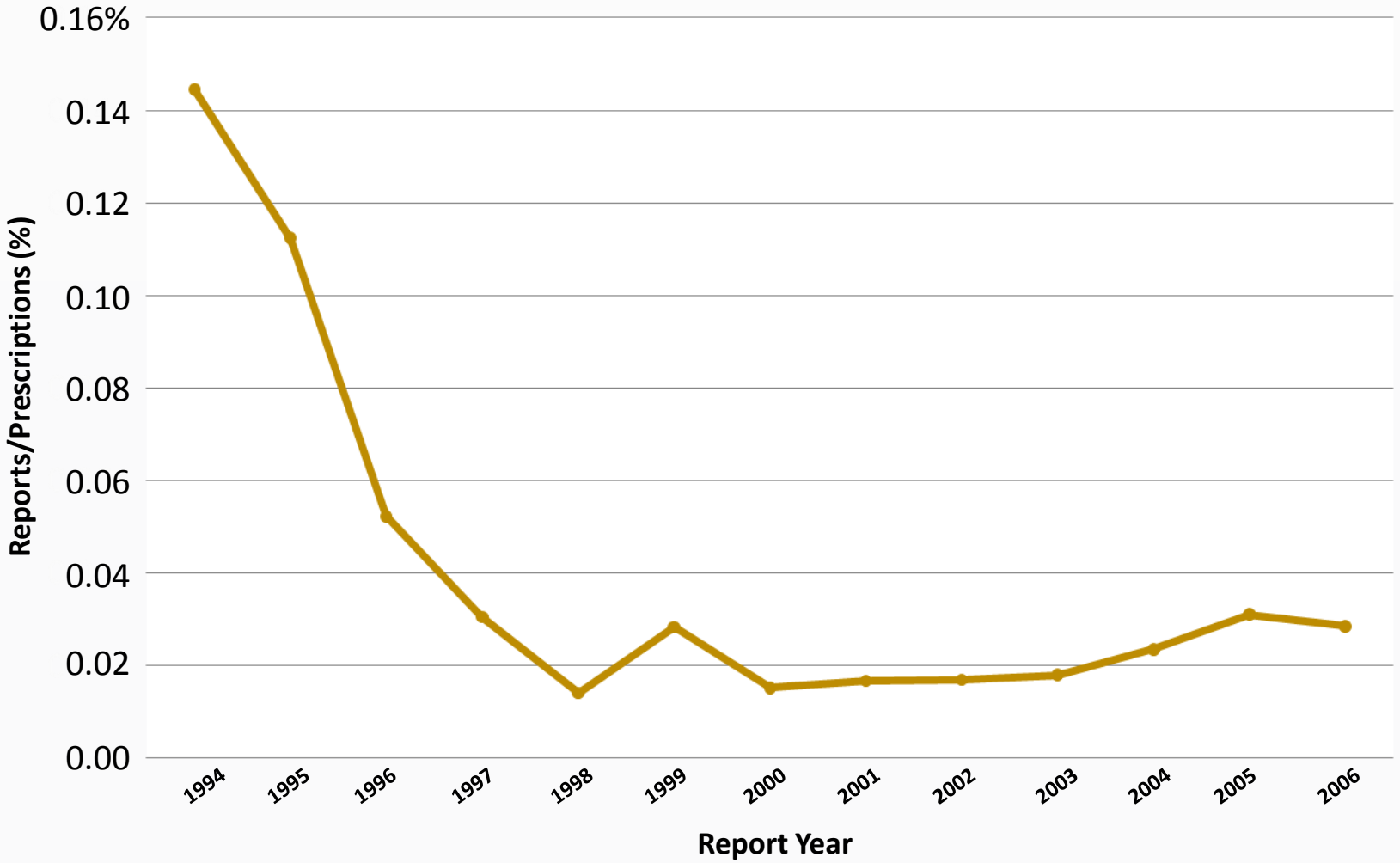
Source: Weiss Expert Report, Figure 1

Neurontin/Gabapentin Prescriptions Over Time



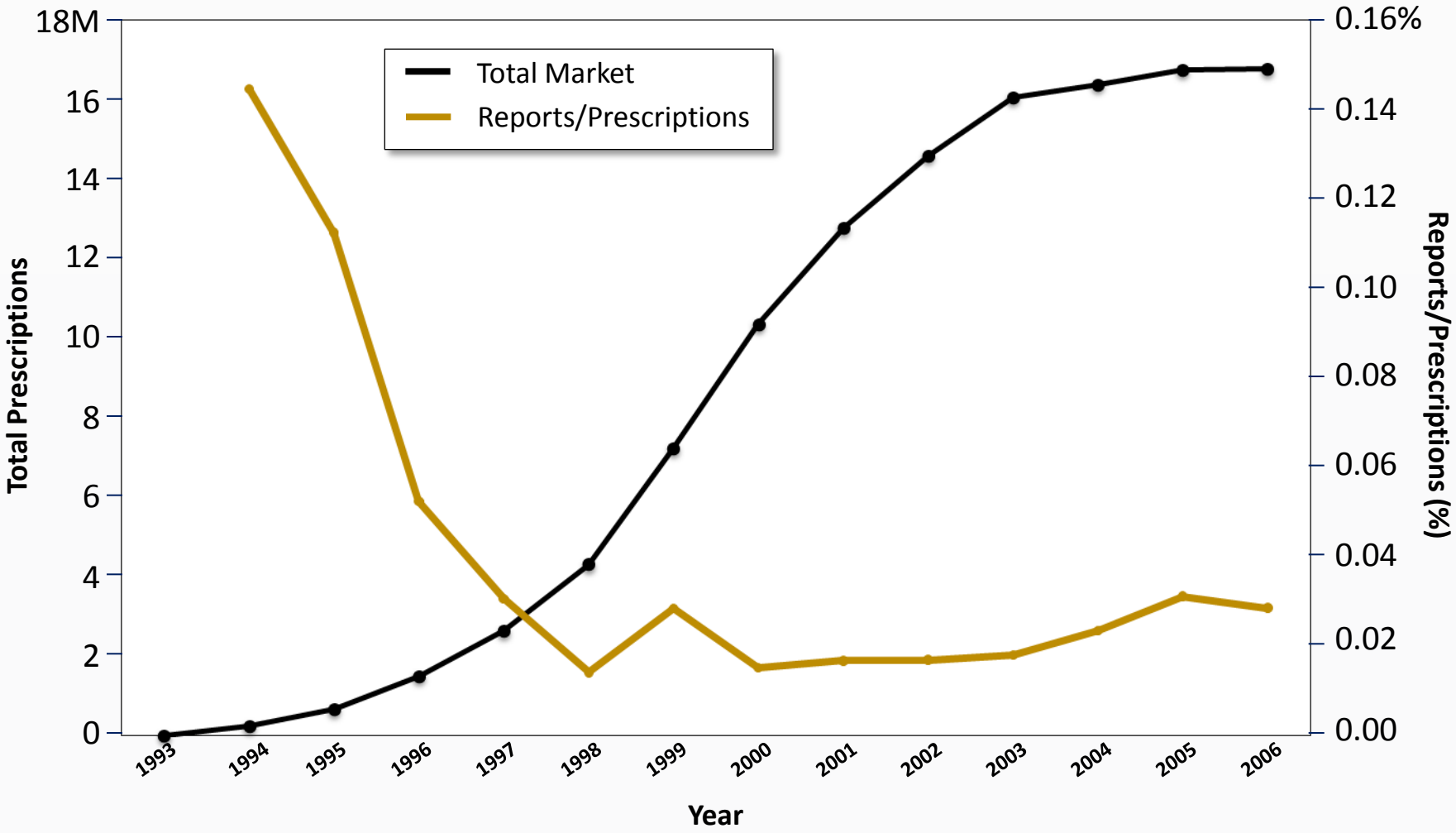
Source: Weiss Expert Report, Figure 2

Gabapentin Reports as a Percentage of Total Prescriptions

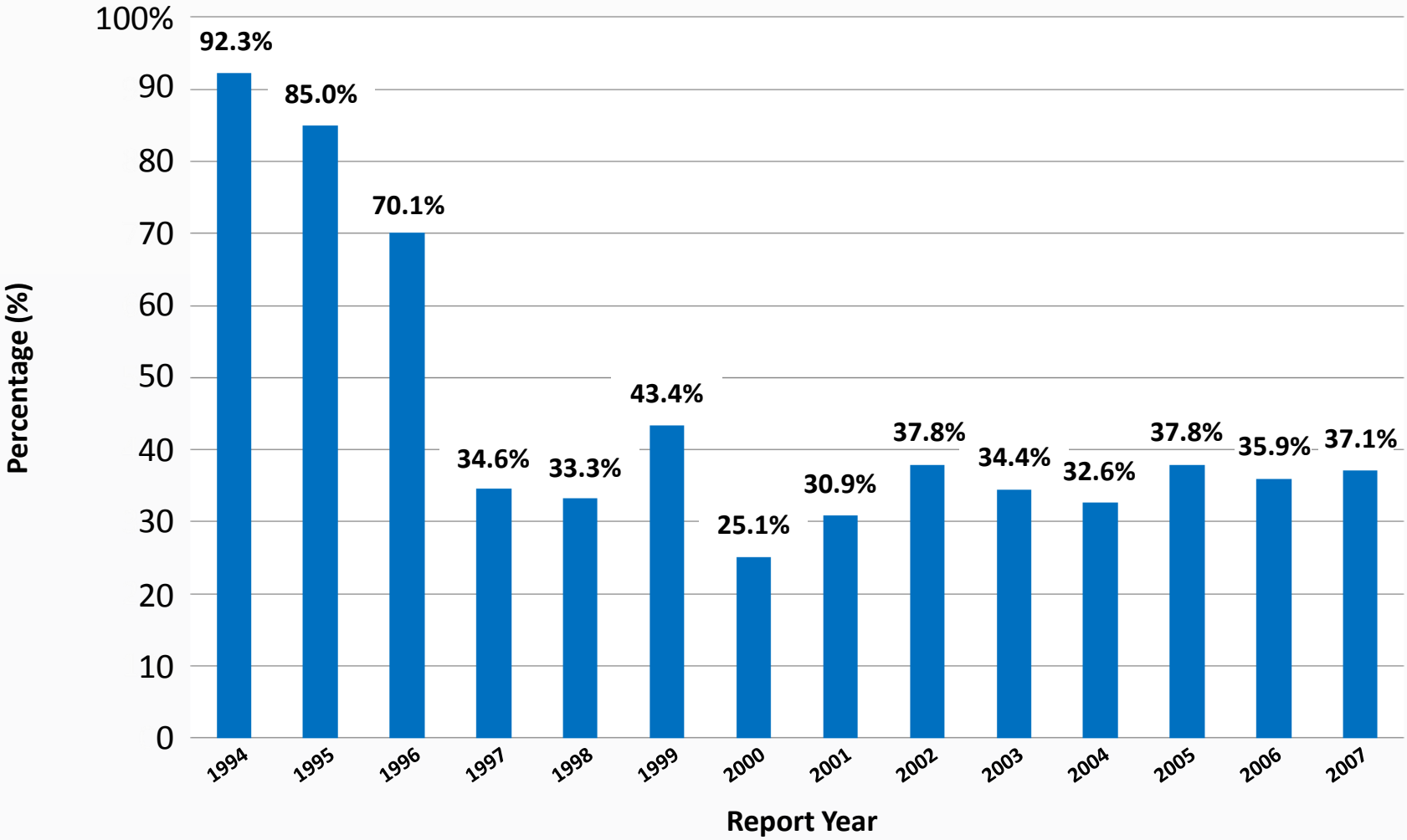


Source: Weiss Expert Report, Figure 3

Gabapentin Reports Decrease As Prescriptions Increase

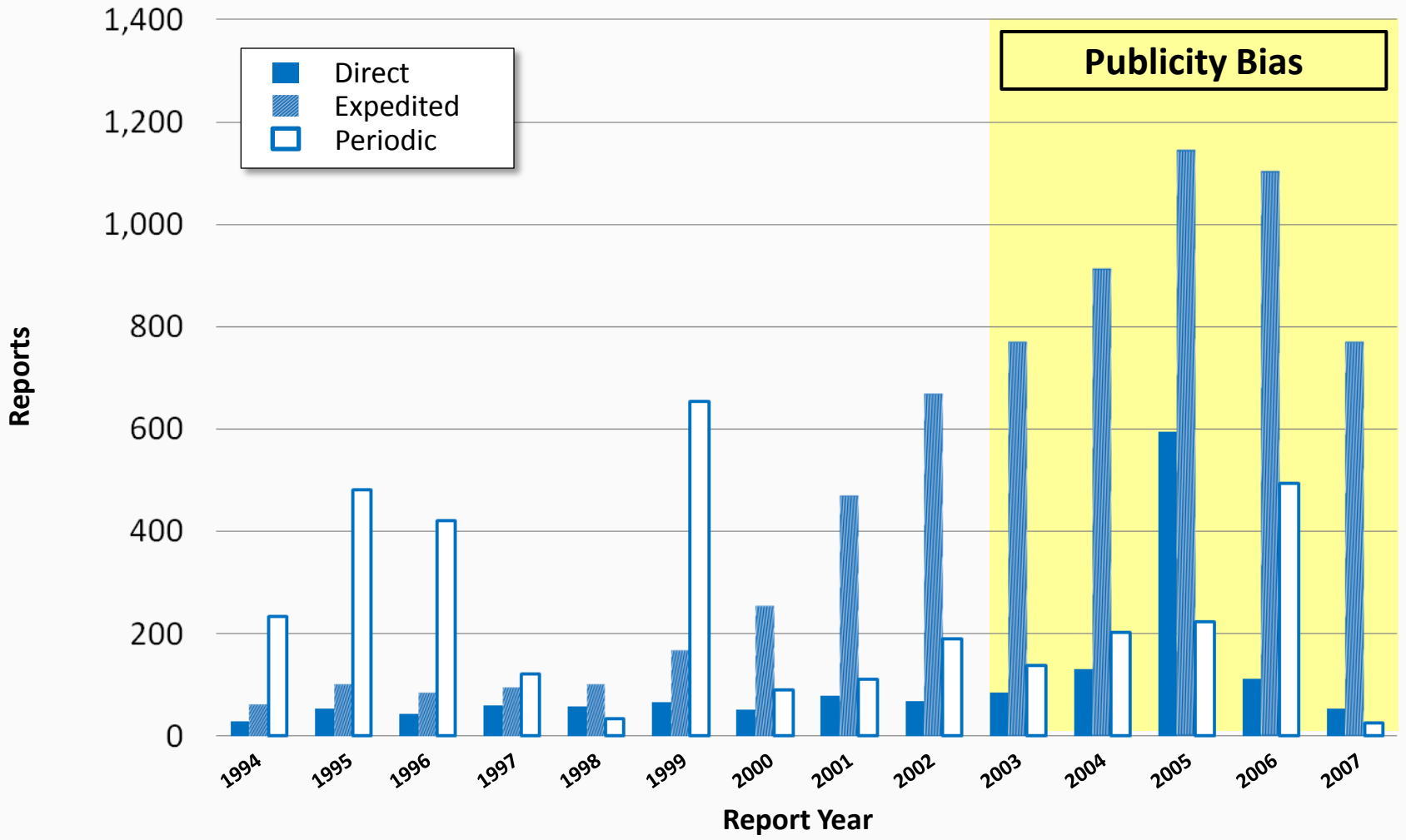


Proportion of Reports In Which Gabapentin 'Was Suspect'



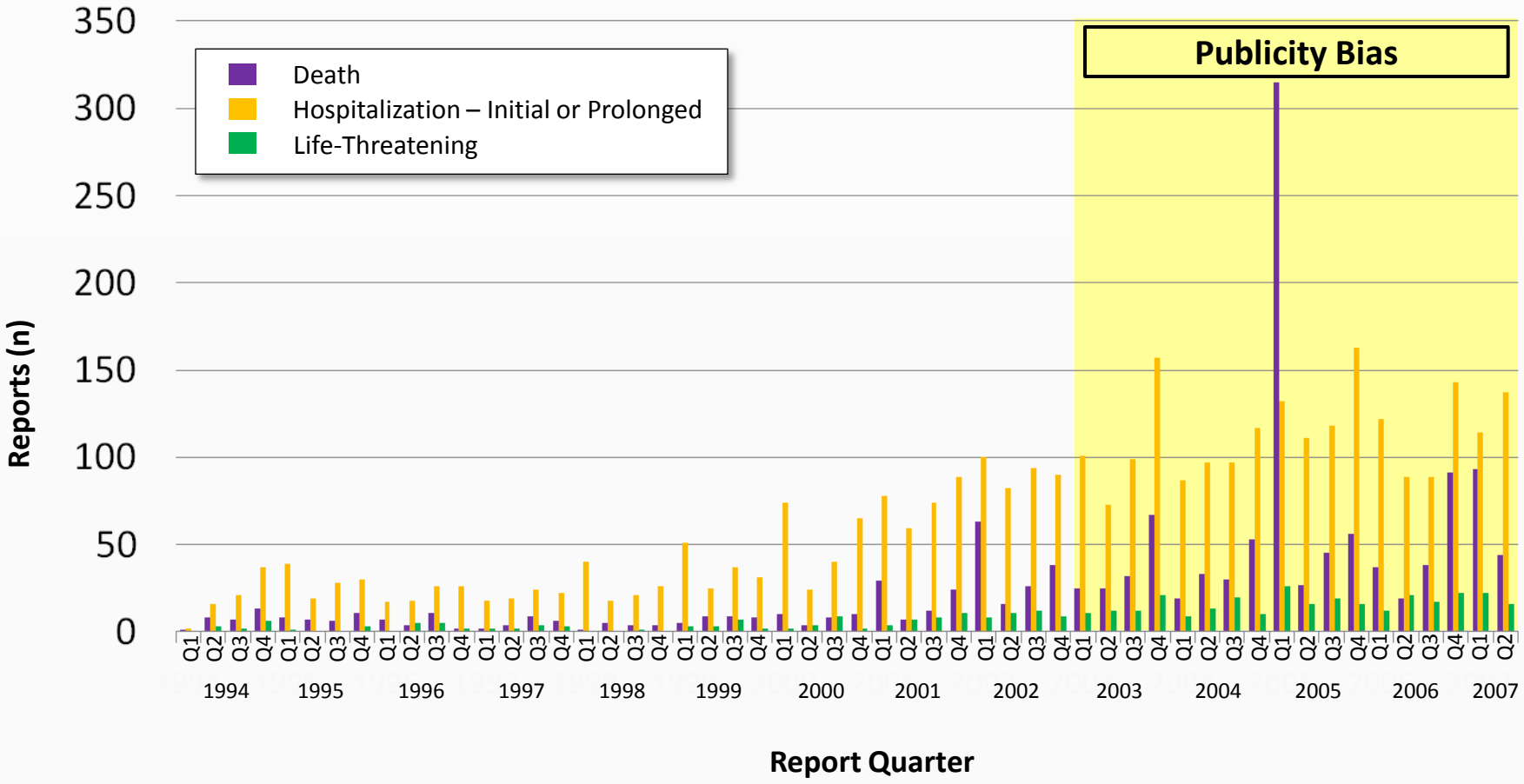
Source: Weiss Expert Report, Figure 4

Gabapentin Reports by Report Type – By Year



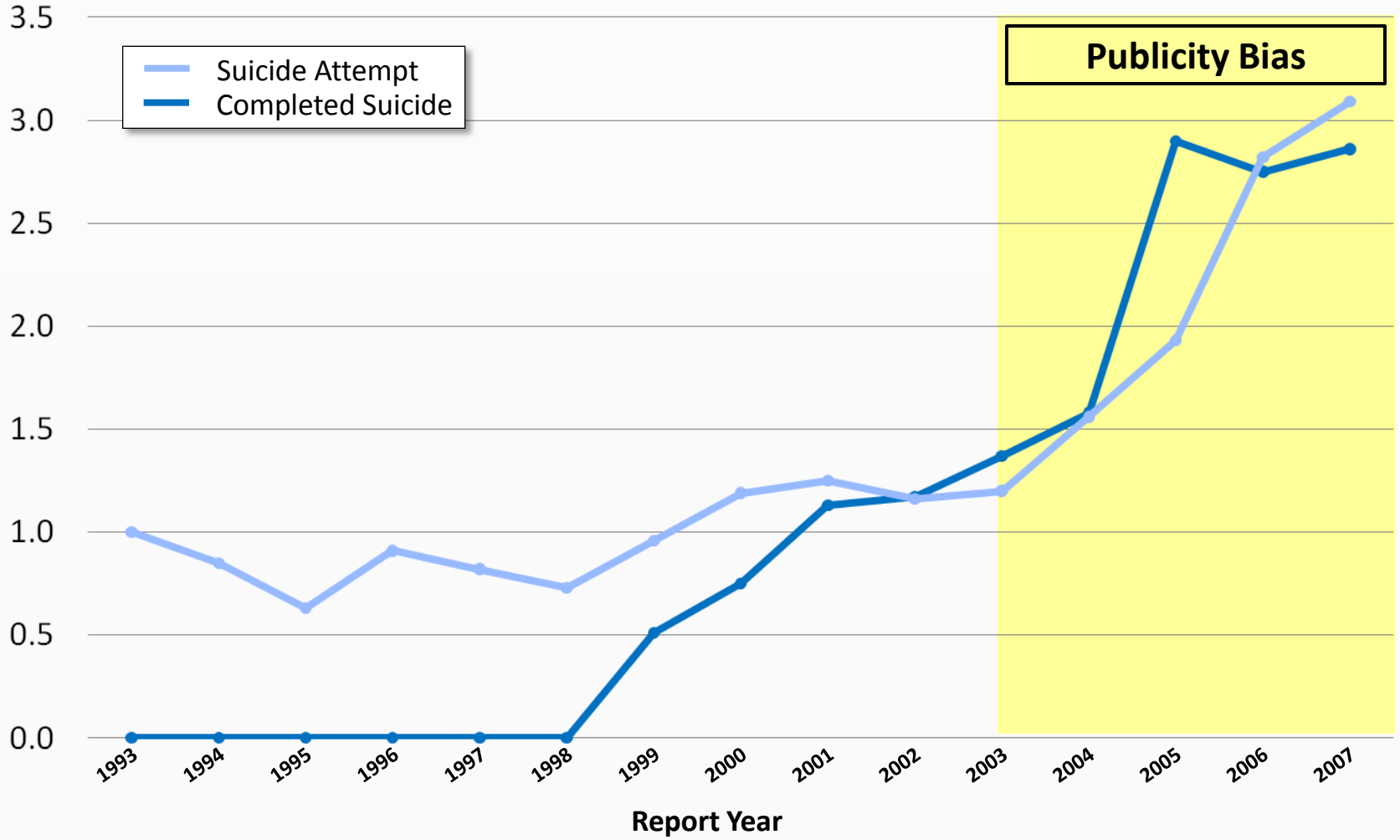
Source: Weiss Expert Report, Figure 6

Gabapentin Reports by Report Type – By Quarter



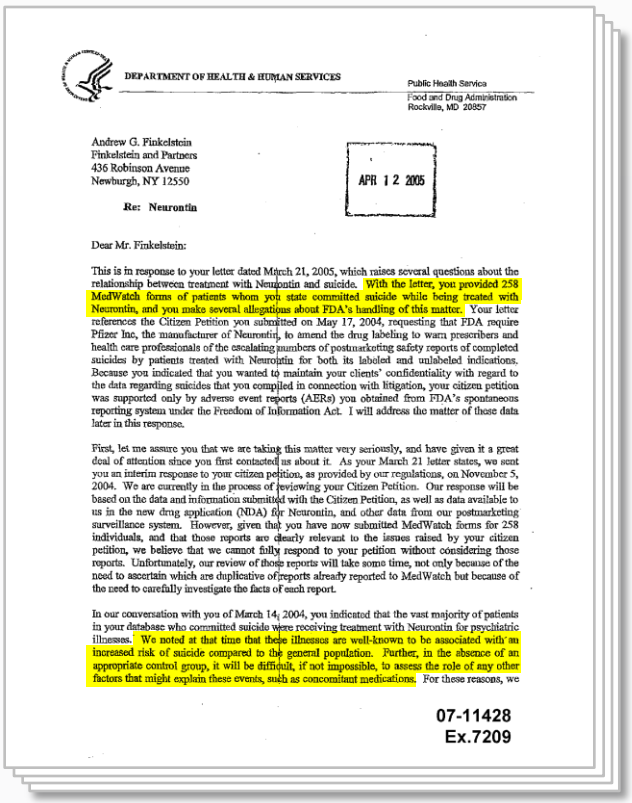
Source: Weiss Expert Report, Figure 7

PRR for Gabapentin: Completed Suicide And Suicide Attempt



Source: Weiss Expert Report, Figure 9

FDA: Controlled Trials Are Only Way to Assess Whether Neurontin Is Associated With Increased Risk of Suicide



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

Andrew G. Finkelstein
Finkelstein and Partners
436 Robinson Avenue
Newburgh, NY 12550

APR 12 2005

Re: Neurontin

Dear Mr. Finkelstein:

This is in response to your letter dated March 21, 2005, which raises several questions about the relationship between treatment with Neurontin and suicide. With the letter, you provided 258 MedWatch forms of patients whom you state committed suicide while being treated with Neurontin, and you make several allegations about FDA's handling of this matter. Your letter references the Citizen Petition you submitted on May 17, 2004, requesting that FDA require Pfizer Inc, the manufacturer of Neurontin, to amend the drug labeling to warn prescribers and health care professionals of the escalating numbers of postmarketing safety reports of completed suicides by patients treated with Neurontin for both its labeled and unlabeled indications. Because you indicated that you wanted to maintain your clients' confidentiality with regard to the data regarding suicides that you compiled in connection with litigation, your citizen petition was supported only by adverse event reports (AERs) you obtained from FDA's spontaneous reporting system under the Freedom of Information Act. I will address the matter of those data later in this response.

First, let me assure you that we are taking this matter very seriously, and have given it a great deal of attention since you first contacted us about it. As your March 21 letter states, we sent you an interim response to your citizen petition, as provided by our regulations, on November 5, 2004. We are currently in the process of reviewing your Citizen Petition. Our response will be based on the data and information submitted with the Citizen Petition, as well as data available to us in the new drug application (NDA) for Neurontin, and other data from our postmarketing surveillance system. However, given that you have now submitted MedWatch forms for 258 individuals, and that those reports are clearly relevant to the issues raised by your citizen petition, we believe that we cannot fully respond to your petition without considering those reports. Unfortunately, our review of those reports will take some time, not only because of the need to ascertain which are duplicative of reports already reported to MedWatch but because of the need to carefully investigate the facts of each report.

In our conversation with you of March 14, 2004, you indicated that the vast majority of patients in your database who committed suicide were receiving treatment with Neurontin for psychiatric illnesses. We noted at that time that these illnesses are well-known to be associated with an increased risk of suicide compared to the general population. Further, in the absence of an appropriate control group, it will be difficult, if not impossible, to assess the role of any other factors that might explain these events, such as concomitant medications. For these reasons, we

07-11428
Ex.7209

April 12, 2005 Letter From FDA to Plaintiff's Lawyers

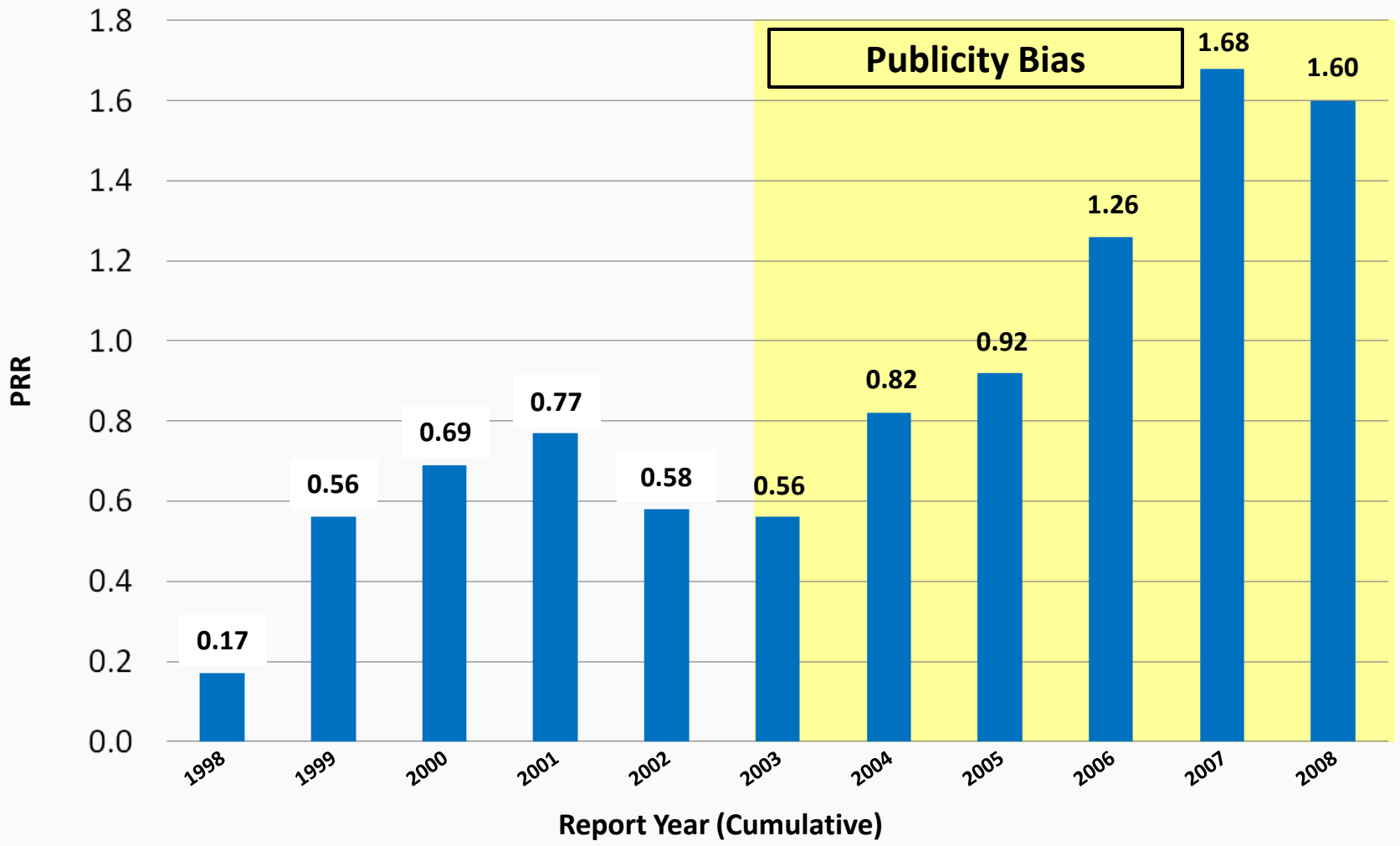
With the letter, you provided 258 MedWatch forms of patients whom you state committed suicide while being treated with Neurontin, and you make several allegations about FDA's handling of this matter.

* * *

We noted at that time that these illnesses are well-known to be associated with an increased risk of suicide compared to the general population. **Further, in the absence of an appropriate control group, it will be difficult, if not impossible, to assess the role of any other factors that might explain these events, such as concomitant medications.**

Source: April 12, 2005 Letter from FDA to Andrew G. Finkelstein (emphasis added)

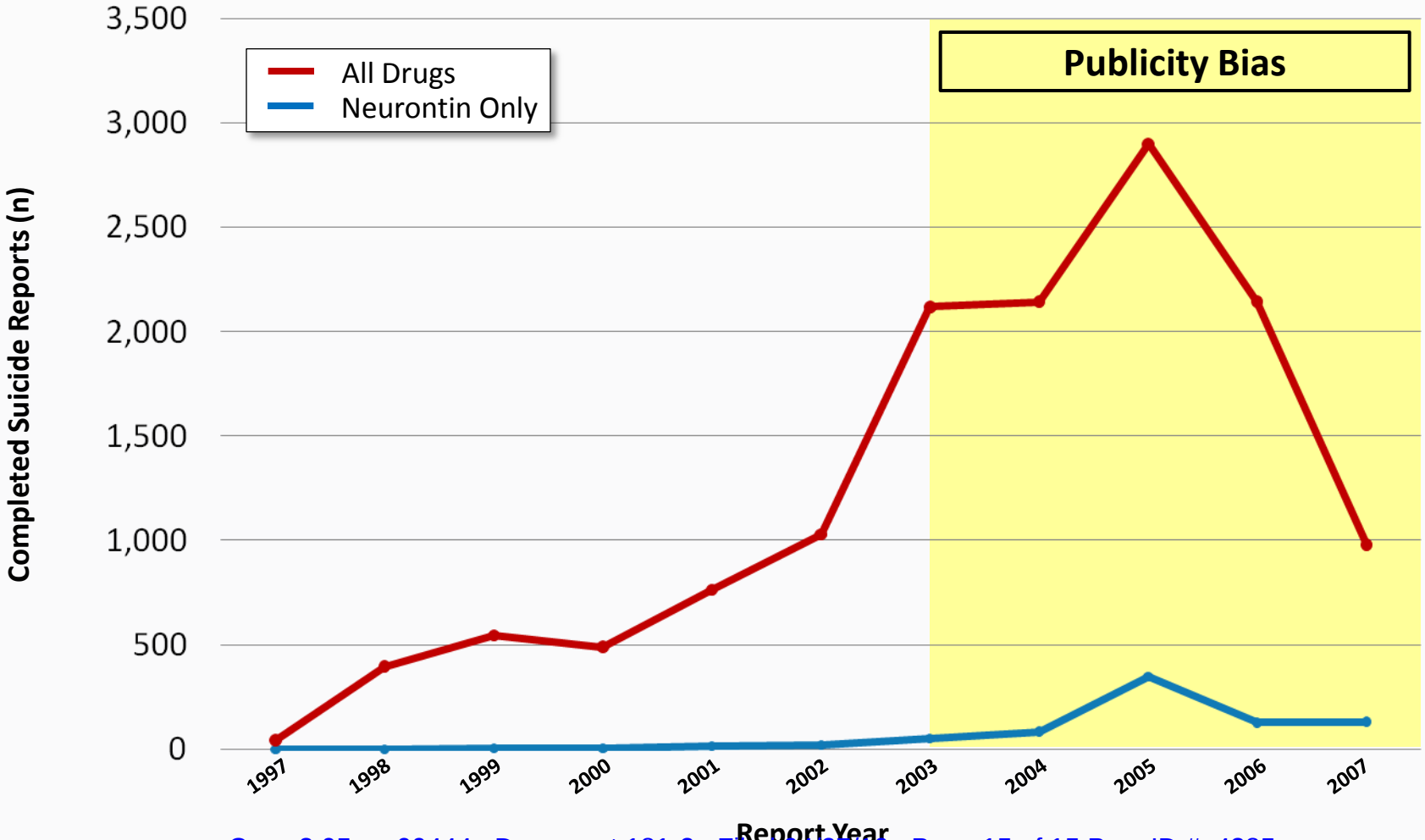
Gabapentin vs. FDA AED Drugs



Source: Weiss Supplemental Expert Report, Figure 1

Completed Suicide Reports

Neurontin vs. All Drugs



Source: Weiss Supplemental Expert Report, Figure 3